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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,091	11/25/2003	Sebastiano Cavallaro	17357.01202US	4892

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EXAMINER

EMCH, GREGORY S

ART UNIT PAPER NUMBER

1649

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/720,091	<b>Applicant(s)</b> CAVALLARO ET AL.	
	<b>Examiner</b> Gregory S. Emch	<b>Art Unit</b> 1649	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 5-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 18-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-21 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's elections without traverse of Group I, claims 1-10 and 18-21, and the species of impaired cognitive performance in the reply filed on 14 August 2006 are acknowledged.

Claims 5-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected subject matter, there being no allowable generic or linking claim.

Claims 1-4 and 18-21 are under examination in the instant office action to the extent that the claims read on the elected species.

### ***Specification***

The disclosure is objected to because of the following informalities: P.23, line 19 contains the typo, "trails".

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a method of increasing cognitive performance in rats, does not reasonably provide enablement for a method of treating attention deficit, epilepsy, schizophrenia, Alzheimer's disease and amnesiac syndromes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims are drawn to a method of treating a condition selected from the group consisting of: impaired cognitive performance, learning deficit, cognition deficit, attention deficit, epilepsy, schizophrenia, Alzheimer's disease and amnesiac syndromes, comprising the step of administering to an individual in need of such a treatment a therapeutically effective amount of Fibroblast Growth Factor-18.

Applicants' specification (e.g., p.10, pp.21-23) discloses a study where rats were implanted bilaterally with guide cannulae into the lateral ventricles and subjected to behavioral analysis 1 week after surgery (day 1). Animals were subjected to a 2-minute training session and were then tested on days 2 and 3 for the ability to find a

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submerged platform to escape the water. On testing days, each animal was subjected to two trials and the escape latency and distance to find the platform were monitored. Ten minutes after the second trial on day 2, FGF-18 or vehicle (saline) was injected ICV. It was concluded that FGF-18 treated animals exhibited an escape latency that was significantly decreased when compared to vehicle treated rats.

Applicants do not disclose any actual or prophetic examples on expected performance of the claimed methods in any specific disease state. Accordingly, it is well known in the art that neurodegenerative diseases, such as Alzheimer's and epilepsy, have different symptoms, pathologies, and etiologies. For example, epilepsy can be caused by a variety of acute or congenital factors, including cortical damage from trauma, stroke, tumors, failure of the cortex to develop properly, congenital vascular malformations, and autoimmune conditions wherein antibodies to glutamate receptors contribute to the pathology (Purves et al; Eds, Neuroscience, 2001, Sinauer Associates, Inc., 2nd Edition, p. 554). Further, no effective prevention or cure exists for epilepsy, although some successful therapy is achieved with altering ion channel conductance, or with more severe cases, removal of cerebral tissue (p.555). Also, Bridler et al. (Swiss Med Wkly. 2003 Feb 8;133(5-6):63-76) teaches that even with the most successful treatment for schizophrenia, i.e., antipsychotic therapy, a significant number of patients relapse or develop partial or full resistance (p.64). Additionally, Vickers (Drugs Aging 2002; 19(7):487-94) teaches, "Alzheimer's disease (AD) is the leading cause of age-related dementia and is set to markedly increase in incidence with the gradual aging of the populations in both developed and developing nations. Along

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with most brain diseases and conditions, there is no effective treatment currently available to reverse, slow down or prevent its course" (first paragraph). Since the claims encompass methods reciting various disease states and given the art-recognized unpredictability of treatment protocols, it would require undue experimentation to treat all of these disease states with one compound, FGF-18.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary to establish a nexus between the claimed methods reciting administration of FGF-18 and the treatment of any disease and/or condition, given the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims which encompass methods of treating multiple neurological diseases or conditions, undue experimentation would be required of the skilled artisan to practice the claimed invention.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap

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between the steps. See MPEP § 2172.01. The omitted steps are: a selection step and a conclusion step.

Claims 1 and 2 are directed to a method of enhancing learning or memory consolidation in an individual which comprises administering an effective amount of Fibroblast Growth Factor 18 (FGF-18). Applicant omitted the selection step for said individual. If the claim language was amended to recite "an individual in need thereof" for example, (as in claims 3 and 18), the rejection may be reconsidered. Additionally, there is no conclusion for the recited methods of claims 1-4 and 18-21.

Appropriate corrections are required.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellsworth et al. (Fibroblast growth factor-18 (FGF18) reduces infarct volume and behavioral deficit after occlusion of the middle cerebral artery in rats, Society for Neuroscience Abstracts, (August 24, 2001; Vol. 27 (No. 2): p.2026).

The claims are directed to a method of enhancing learning in an individual which comprises administering an effective amount of Fibroblast Growth Factor 18 (FGF-18).

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Ellsworth et al. teaches intravenous infusion of FGF-18 that reduced cerebral infarct volume and decreased deficits in reference and working memory, exploratory behavior and motor activity in rats after middle cerebral artery occlusion, thus meeting the limitations of claims 1-4 and 19. It is noted that for IV administration, the skilled artisan must administer FGF-18 in a pharmaceutically acceptable carrier, (such as saline, for example). Thus, the Ellsworth et al. reference also meets the limitations of claim 18. It is well known in the art that the hippocampus is involved in memory consolidation and working memory. Therefore, it is also well known to those of skill in the art IV infusion of a drug, in this case FGF-18, would inherently be increased in the brain (and therefore in the hippocampus) if improvement in cognition were achieved after treatment. Thus, the Ellsworth et al. abstract also meets the limitations of claims 20 and 21, i.e., wherein the composition is administered in an amount effective to increase FGF-18 levels in the subject's brain and hippocampus. Thus, since the reference teaches all the elements of the claims, claims 1-4 and 18-21 are anticipated by Ellsworth et al.

### ***Conclusion***

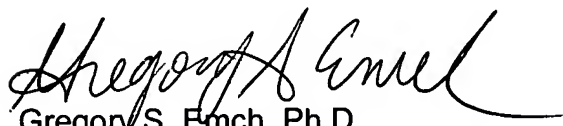
No claims are allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 9AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Gregory S. Emch, Ph.D.  
Patent Examiner  
Art Unit 1649  
29 August 2006

  
JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER